aa^{84} is a hydrophobic or small amino acid;

wherein

the sequence in the brackets may optionally be absent or truncated at any [peptide type] bond within the brackets.

18. (Amended) A method for extending the period of acceptance by a recipient a transplant from an allogenic or xenogenic MHC [unmatched] donor, said method comprising:

administering to said donor in accordance with a [predetermined] therapeutically effective regimen[,] and in an amount effective to extend the period of acceptance of said transplant, the compound of claim 1;

whereby the period of acceptance of said transplant is extended.

19. (Amended) The method of claim 18, wherein said compound is administered in combination with a subtherapeutic dosage of an immunosuppressant, and said period of acceptance is extended as compared to the period which would have resulted from the administering of [the] said immunosuppressant as said subtherapeutic dosage in the absence of said compound.

REMARKS

Claims 1-26 are pending. By way of the present amendment, claims 1, 18 and 19 have been amended. Claims 22-26 remain pending, but are withdrawn from consideration as a non-elected invention under a restriction requirement.

Support for the amendments to the specification introduce no new matter and their entry is respectfully requested. The inadvertent second recitation of "N-terminal" at page 4, line 26 is an obvious error on its face since an N-terminal, by convention, is the portion of the molecule amidated. It is further obvious that this recitation is an obvious error in view of the correct

recitation of "C-terminal amidated or esterified forms" at each of: page 3, line 13; page 9, lines 19-21; and in claim 1 as originally filed.

Support for the correction of the inadvertent recitation of "Example 3C" is obvious on its face in view of the lack of a section C in Example 3. However, a reading of the context of "Example 3C" make clear that the reference is to the protocol presented in Example 2C.

These corrections to the specification are minor, but in the interest of providing a correct enabling disclosure, Applicant wishes to bring these inadvertent errors to the Office's attention.

Support for the amendments to the claims can be found, for example, in the claims as originally filed and at page 3, lines 7-8; page 4, lines 15-20; page 13, lines 27-28; page 15, lines 13-15 and 18-24; page 28, lines 10-11; and page 31, line 7. The amendments to the claims add no new matter and their entry is respectfully requested. Based on the above amendments and the following remarks, Applicants respectfully requests that the Examiner reconsider the rejections of the claims, that he withdraw same, and that he pass the application to issue.

Applicant's Telephonic Interview with the Examiner of November 25, 1997.

At the outset in response, Applicant expresses appreciation to the Examiner for a very productive telephonic interview held on November 25, 1997, which included Examiner T. Cunningham; Dr. C. Clayberger, a co-inventor; and the Applicant's undersigned representative.

The substance of the interview included a review and discussion of the Office Action mailed July 21, 1997; and Applicant's proposed amendment to the claims, which substantially is reproduced in this response. The Examiner and Applicant discussed the art cited under 35 U.S.C. § 103(a); the Examiner's concerns relating to the rejection of the claims under 35 U.S.C. § 112, first and second paragraphs; and Applicant's comments in response to the Office Action, specifically to each of the rejections as stated therein, which comments and remarks have been substantially reproduced in this response thereto.

Restriction Election with Traverse.

Applicant confirms the election with traverse to prosecute the invention of Group I, claims 1-21, as provisionally made during a telephone interview between the Examiner and Applicant's representative on May 19, 1997. The Examiner has made a three-way restriction requirement: Group I, claims 1-21 drawn to peptide products; Group II, claims 22-25 drawn to nucleic acids; and Group III, claim 26 drawn to antibodies. This restriction is made upon the basis that the inventions are distinct, each from the other, in that each may be practiced separate and apart from the practice of the other(s). The Examiner concludes that these inventions are unrelated "if it can be shown that they are not disclosed as capable of use together or they have different modes of operation or they have different functions, or they have different effects." However, these embodiments of the claimed invention have been disclosed as capable of use together.

Applicant traverses this restriction requirement on the following grounds. Restriction of an invention is within the discretion of the Commissioner, if the inventions are independent and distinct and a search of the inventions would place a serious burden upon the Examiner if the restriction is not required. (See 37 C.F.R. 1.142 and MPEP 803) Here, the Examiner has failed to state what burden, if any, would ensue were a restriction not made. This failure to satisfy the second prong of the MPEP 803 test establishing when a restriction is proper, therefore, renders this restriction improper and void.

These inventions as presently claimed clearly recite that they are capable of use together, in that the DNA molecule of claim 22 comprises a nucleotide sequence that encodes the peptide of claim 21, which depends upon claim 1. Further, the antibody of claim 26 is specifically reactive with the peptide of claim 1. The genetic basis of expression provides the inter-functional relationship between the genetic nucleic acid sequence that encodes a peptide sequence as well as encoding peptide sequences that are expressed as antibodies, which in turn are able to specifically bind to other peptide sequences. For these reasons, Applicant respectfully requests that the Examiner withdraw this restriction.

Declaration of Dr. Carol Clayberger.

Applicants are submitting a copy of a Declaration by Dr. Carol Clayberger that was prepared and filed on April 17, 1996, in the parent application US Serial No. 08/222,851 ("'851 application"), whose contents have been previously incorporated by reference. This declaration was prepared in response to an Office action by the present Examiner in the parent '851 application. Although the Declaration addresses specific comments provided by the present Examiner in the other office Action, Applicants respectfully assert that the positions taken by the Examiner in the two cases are the sufficiently similar to support the Examiner's consideration of the substance of the Declaration in the present case.

The Declaration discusses data that is provided in the parent '851 application. Applicants are attaching a copy of the Examples that are referenced in the Declaration as a means of making the data contained therein of record.

Objection to Specification.

The Examiner has objected to the specification because the oath or declaration is allegedly defective for failure to acknowledge Applicant's continuing duty to disclose material to the prosecution of this application under 37 CFR 1.56(a). The Examiner has further directed Applicant to submit a replacement oath or declaration or alternatively state the intention to waive claim of priority.

Applicant considers the declaration executed by all of the inventors as filed on September 10, 1996 to be correct. Applicant's acknowledgement of the duties under 37 CFR 1.56 is clearly present in this declaration. Applicant would appreciate the Examiner pointing to specific authority upon which he is relying to require Applicant to submit a replacement declaration or make further statement on this record regarding this matter.

Rejection of claims under 35 U.S.C. §112, second paragraph.

Claims 1-21 are rejected under 35 U.S.C. §112, second paragraph as indefinite for failing to particularly point out and distinctly claim the subject matter that applicant regards as the invention.

Specifically, the Examiner notes that recitation of "MHC unmatched donor" is considered vague and indefinite. Applicant traverses this rejection since MHC matched or unmatched is an art recognized phrase, which is clearly a reference to whether or not an antigenic phenotype is homogenic or allogenic in regard to MHC antigen. For example, in U.S. patent No. 5,667,967 (issued September 16, 1997 on an application filed May 21, 1993 claiming priority to May 1, 1990), at column 11, lines 43-45 is recited:

> "Alternatively, one may have a stored supply of T-cells of the appropriate variable region and either matched or unmatched as to MHC, particularly Class I."

However, in the interests of more fully clarifying what Applicant considers to be the invention, the claims now recite: "transplant from an allogenic or xenogenic MHC [unmatched] donor".

The Examiner states that recitation of "predetermined regimen" is considered to render the claims unclear. Applicant traverses this rejection in view of the written disclosure which provides clear teaching on what constitutes a predetermined regimen. For example, see page 14, line 3 to page 16, line 17, and particularly at page 14, lines 16-17, where it is noted that:

> "It is found that various regimens may be employed effectively, so that no particular regimen can be specifically defined."

The disclosure provides clear guidance to enable the skilled artisan to develop a specific regimen prior to the transplantation. However, in the interest of further clarifying the claimed invention, the present claims recite: "in accordance with a [predetermined] regimen[,] and in an amount effective".

The Examiner further notes that recitation of each phrase: "extend the period of acceptance" and "inhibit transplant rejection" is considered to render the claims vague and indefinite.

Applicant traverses each of these rejections. These phrases delineate in the claims the reduction or elimination of immunological rejection of transplanted tissue. Such terms would be well understood by the skilled artisan. Further, the claims are read in light of the specification, which provides clear guidance as to their metes and bounds. For example, in the specification see generally page 1, lines 22-25; and specifically page 13, lines 25-26, where is disclosed:

> "The immunomodulating activity of the compounds of the invention makes them useful in preventing rejection of transplants and in the treatment of autoimmune diseases."

The Examiner notes that is it unclear how to objectively measure the extension of transplant acceptance and inhibition of rejection. However, the skilled artisan would fully appreciate the indicia of host-graft rejection, a few examples of which are presented in the Examples. "Rejection was manifested by erythema, continuous serous exudation, ulceration or allograft necrosis."(specification at page 28, lines 10-11) Further, Applicant disclosed, for example, the mouse foot pad assay to assess alloreactivity *in vivo*:

> "To assess whether the peptides could affect alloreactivity *in vivo*, we tested their effects on the accumulation of cells in the draining lymph nodes following injection of nonself spleen cells into footpads as described above. "(specification at page 30, lines 6-8)

Also, Applicant disclosed that "[G]raft function was monitored by daily abdominal palpation, and rejection was scored as complete when the palpable ventricular contractions ceased."(specification at page 31, lines 6-7). Clearly, these are objective indicia of extending the period of acceptance and measuring inhibition of rejection.

The Examiner further considers the recitation of "subtherapeutic dosage" to render the claims vague and indefinite. Applicant traverses this rejection on the grounds that the phrase has

clear meaning in the art and is well delineated in the written description. For example, in the specification at page 15, lines 13-15 and lines 18-24, Applicant teaches:

> "By subtherapeutic dosage is intended that in the absence of the peptide, the graft would be rejected in a majority of patients within 100 days, usually within 30 days, and more usually within 20 days." (lines 13-15)

> "The subtherapeutic dose will be not less than about 5% of the therapeutic dosage, usually not less than about 10%, more usually not less than about 25%, and usually not greater than about 75%, more usually not greater than about 60%. Where combinations are used, the subtherapeutic dosage is primarily directed to the drug(s) which have significant side effects, although there is a substantial interest in minimizing the effect on the immune system. In referring to a subtherapeutic dosage, is intended a bolus amount, since a direct comparison is difficult, where the subject regimen is terminated within a short period of the transplantation."(lines 18-24)

The Examiner additionally considers the recitation of "immunosuppressant" to render the claims unclear. Applicant respectfully points out that the terms used in the claims are to inform the ordinary skilled artisan as to the metes and bounds of the claim. An "immunosuppressant[s]" is recognized as compounds "which generally debilitate the immune system."(specification, page 1, line 20).

The Examiner invited Applicant to point to the specification where the term is defined. Since this term is used consistent with its art recognized meaning, Applicant has no duty or obligation to further define this term. However, in the interests of expediting the prosecution of this application, Applicant refers the Examiner to page 15, lines 8-17, whereat is recited:

> "As part of the regimen, an immunosuppressant drug can also be administered, generally at or subsequent to the transplant, either by itself, or in conjunction with the peptide, particularly where the peptide is administered after the transplantation. A subtherapeutic dose of the immunosuppressant compound is employed, **where the immunosuppressant may be a single agent or a combination of agents**, where the combination is below a subtherapeutic dosage.

> By subtherapeutic dosage is intended that in the absence of the peptide, the graft would be rejected in a majority of patients within 100 days, usually within 30 days, and more usually within 20 days. **Various immunosupressants are known, such as** cyclosporin A, FK506, antibodies for plasma membrane proteins associated with graft rejection, such as antibodies to CD4, CD8, CD2, LFA-1, ICAM-1, CD28, and the like."(emphasis added)

The Examiner has also rejected the claims over the use of the phrase "peptide-type" compounds, which the Examiner finds unclear. The Examiner invited Applicant to point to the specification where this phrase is defined. Again, Applicant duly notes that Applicant's use of this phrase is consistent with the art and therefore Applicant is under no obligation to provide further definition. Although, Applicant is pleased to refer the Examiner to the specification at page 3, line 12 to page 4, line 5; page 4, line 21; page 5, line 25 to page 6, line 2; and page 10, lines 1-4. However, in the interests of expediting the prosecution of this application, this term has been deleted from the claims without prejudice.

A "variant" of a peptide-type compound is used consistent with the disclosure of the specification:

> "'variants', i.e., peptide-type compounds which differ from those specifically set forth above by conservative substitutions which do not destroy the immunomodulating activity of the compound. As to variants, by "conservative substitution" is meant that an amino acid which is of the same general group as that for which substitution is made replaces the referent amino acid. The replacing amino acids may or may not be gene-encoded. They may also include either D or L-isomers where relevant." (page 6, lines 7-13)

The Examiner has found that "hydrophobic or small" amino acids renders the claims unclear. Applicant refers the Examiner to the specification, at page 6, lines 23-25, to wit:

> "Hydrophobic: The residues are not charged at physiological pH and the residue is repelled by aqueous solution so as to seek the inner positions in the conformation of a peptide in which it is contained when the peptide is in aqueous medium."

At page 7, lines 22-23:

"Hydrophobic: Tyrosine, Valine, Isoleucine, Leucine, Methionine, Phenylalanine, Tryptophan."

At page 7, lines 1-4:

"This description also characterizes certain amino acids as "small" since their side chains are not sufficiently large, even if polar groups are lacking, to confer hydrophobicity. "Small" amino acids are those with four carbons or less inclusive of the carboxyl when at least one polar group is on the side chain and three carbons or less when not."

The claims are rejected for the recitation of "immunomodulating", which is considered to render the claims indefinite. Applicant traverses this rejection on the grounds that the specification discloses that this term is used consistent with the art and is clear to the ordinary skill artisan. For example, see page 6, lines 3-6:

"By "immunomodulating activity" is meant that the compound can be shown to inhibit CTL-mediated lysis in the cytotoxicity assays set forth in Example 1 below and/or inhibits the proliferation of purified T cells in response to anti-CD3 according to the assay described in that example."

Claim 1 has been amended to recite: "lymphocyte immunomodulating activity" to more particularly point out the type of immunomodulation.

The claims are rejected as unclear regarding whether the language of claim 1 is open or closed and regarding whether the compound is limited to peptides of 60 amino acids or less. Claim 1 has been amended to more particularly point out what Applicant intends to claim. The limitation of "wherein said compound further comprises from at least 12 [of] up to 60 amino acids" is supported at page 4, lines 15-20, which discloses the minimum number of amino acids is six (6), but that the subject compounds are dimeric and therefore are comprised of at least twelve (12) amino acids up to 60.

Rejection of the claims under 35 U.S.C. §112, first paragraph.

The claims are rejection under 35 U.S.C. § 112, first paragraph as the claims are considered enabling only for those particular peptides such as the sequences demonstrated to inhibit cytolysis on pages 21 *et seq.* of the specification. Applicant respectfully traverses these rejections based upon the following remarks.

The claims are rejected upon 10 separate functional bases. Claims 1-17 and 20-24 and 26 are directed to compositions of matter, whereas claims 18-19 are drawn to methods of use and 25 is directed to a method of genetic expression to make the peptide of claim 21. A functional limitation in claim 1 requires that the compositions of matter each have lymphocyte immunomodulating activity. Applicant respectfully maintains that these multiple rejections for lack of enablement of claims 1-17, 20-24 and 26 drawn to compositions of matter and claim 25 drawn to method of genetic expression are improper. The compositions have been fully enabled by the specification and the preparation and testing of at least 17 separate peptides, each with its own unique amino acid sequence. (See Table 1, at page 21) Further, Applicant disclosed specific amino acid substitutions (See pages 21-22); serine substitution (See pages 22-23); and D-amino acid substitution (See page 23). Applicant has disclosed three separate assays: (1) Inhibition of Lysis by Established CTL (See pages 21-23); Inhibition of T cell Proliferation (See pages 24-26); Lymph Node Proliferation Assay (See page 30); Heart Allograft in Rat Model (See pages 31-34); and Heart Allograft in Mouse Model (See pages 34-36).

The legal test for enablement has been clearly stated by the Court of Appeals for the Federal Circuit in *In re Wands,* 8 USPQ 2d 1400 (Fed. Cir. 1988). The Court of Appeals for the Federal Circuit held that the factors that should be considered when determining whether a particular amount of experimentation is undue or not is "(1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art and (8) the breath of the

claims." Applicants respectfully assert that the making and testing of any of the limited number of peptides that fall within the claims requires only routine experimentation. Accordingly, under the proper test, the claims are enabled for the scope recited.

With regard to claim 25 drawn to methods of genetic expression to make the claimed peptide, such routine expression of genetic sequences was well within the ordinary skill of the art at the time of the claimed invention.

Similarly, with regard to claims 18 and 19 drawn to methods of use of the claimed compounds, Applicant respectfully maintains that in view of the clearly defined compounds of the claims and the number of assays disclosed in the specification, the skilled artisan would not find the testing and use of said compounds undue experimentation, but rather routine screening and optimization.

Each specific rejection of the claims under 35 U.S.C. § 112, first paragraph is addressed by the following remarks.

1. *In vivo* usage

The Examiner has expressed that in view of mechanical barriers and serum proteases as well as "immunological clearance mechanisms", would result in undue experimentation for the routine artisan to be able to practice the claimed compounds and methods. However, Applicant has taught the use of the claimed compounds to modulate the immunological response associated with host-graft rejection in two separate animal models: rat and mouse. (See pages 31-36). If the Examiner maintains this rejection, he is respectfully requested to provide specific scientific information or references to support the rejection.

> "Applicant's disclosure must be given the presumption of correctness and can be challenged by the PTO only upon the basis of factually supported doubts." *In re Marzocchi,* 439 F.2d 220, 169 USPQ 367 (CCPA 1967)

These two animal models provide a clear and enabling disclosure of the claimed invention *in vivo*. Further, this invention is drawn to dimeric peptide sequences that interact with ligands whose sequences, themselves are highly conserved.

Applicants respectfully assert that the application as well as the attached declaration of Dr. Carol Clayberger: 1) provides sufficient *in vitro* data to demonstrate non-allele specific CTL inhibitory activity for peptides comprising residues 75-84 of two of the six known human HLA-B alpha-1 domain alleles, 2) demonstrates that routine procedures can be used to generate compounds comprising the amino acid sequence of residues 75-84 of any MHC Class I HLA-B allele, regardless of the source, 3) demonstrates that routine procedures can be used to generate peptide compounds falling within the formula of claim 41 and 4) provides *in vitro* and *in vivo* results that demonstrate the cross mammal and non-MHC specific activity of members of the recited peptides. The results that demonstrate the above have been summarized in the attached Declaration by Dr. Carol Clayberger that was prepared and submitted in the parent application US Serial No. 08/222,851.

2. Xenotransplantation

The Examiner concludes without further support or by reliance upon any scientific reference that one of skill in the art would require undue experimentation to practice the claimed invention relating to xenographs because "one with skill in the art would not expect that MHC protein sequences from one species (e.g., the HLA molecules of humans) would be capable of blocking immune responses in another species." However, it appears that the Examiner is not challenging that the claimed invention would be enabled where a xenograft from a non-human donor species were made into a human species recipient. Clearly the donated xenograft would be considered foreign by the human recipient. Therefore, Applicant respectfully maintains that the skilled artisan would expect the claimed invention to be enabled for a non-human xenograft donor

to human recipient. It is unclear why the reciprocal xenograft (human donor to non-human recipient) would be contemplated by the skilled artisan in the first place. However, the Examiner is requested to provide a scientific reference or reasoning to support this rejection if maintained.

One of the Examiner's position is that one with skill in the art would not expect that MHC protein sequences would be effective in inhibiting CTLs that are not MHC matched. In the attached Declaration from Dr. Carol Clayberger, Dr. Clayberger states that the results provided in the specification as well as an accompanying scientific reference of Nisco, demonstrated that peptide compounds comprising residues 75-84 of human MHC I proteins are protective in an art recognized rat heart allograft model. Since the human peptides are active in rats, and the one sequenced rat MHC Class I HLA-B alleles have less than 70 and 50% homology to the human B7 and B2702 alleles respectively, the evidence of record clearly indicates that the peptides do not need to be MHC matched to be effective in inhibiting CTL activity.

The questions raised by the Examiner are directed to the predictive value of Applicants observations with regard to other members of the HLA-B family of proteins, to peptides that fall within the formula recited in claim 41, and the degree of experimentation that would be required to make and test other members of the protein compounds recited in the claims. Applicants' contend that the focus of an enablement rejection is not predictability but whether one skilled in the art could practice any particular member encompassed by the claims without undue experimentation.

3. Allotransplantation

The claims are rejected as lacking enablement because the Examiner considers that they encompass the inhibition of CTL's which do not share MHC specificity with the administered peptide. Applicant respectfully maintains that the specification clearly provides sufficient guidance to the ordinary skilled artisan to practice the claimed invention.

Applicant has taught that there is variation; how to screen for variation; and the location of those amino acids that play a critical role. Therefore, the skilled artisan is enabled to conduct routine experimentation following the instant specification to practice the claimed compounds.

The need to conduct routine experimentation does not form the basis for a rejection of the claims under 35 U.S.C. §112, first paragraph. Rather, it is if the skilled artisan would be required to conduct undue experimentation that underlies an enablement rejection.

4. Regimen

The claims are rejected for failing to provide an enabling disclosure for a therapeutically effective regimen. The Examiner considers that without a recitation of specific ordered steps and route of delivery, the claimed methods would require undue experimentation. The claims have been amended to add the further limitation of a therapeutically effective regimen. The claims as originally filed provided for a "predetermined" regimen, which was considered to render the claims vague and indefinite. The current limitation is clearly enabled by the instant specification and certainly reflects the fact that that multiple therapeutically effective regimens are contemplated by the claims, provided the regimen demonstrates therapeutic effectiveness. (See page 14, lines 16-17)

The specification discloses at pages 13-17, several therapeutically effective regimens. For example, the regimen may consist of bathing an organ to be transplanted in one or more of the claimed compounds as well as the claimed compounds may be administered prior to, at and subsequent to the day of the transplantation. The claimed compounds may be administered along with a subtherapeutic dose of an immunosuppresant subsequent to the transplant. Various formulations may be employed depending upon the treatment intended.

The regimen could follow that taught in the Examples concerning the inhibition of host-graft rejection in two separate animal models: rat and mouse. (See pages 31-36).

5. Diverse peptides

The claims are rejected as lacking enablement for those sequences not related to the human MHC Class I HLA-B alpha-1 domain. The Examiner observes that the specification teaches at pages 21-22 that the difference of only three residues between the sequence of HLA-B2702.75-84 and HLA-B2705.75-84 is sufficient to alter the activity of these peptides. However, Applicant respectfully maintains that it is just such teaching that enables the present claims.

Applicant has taught that there is variation; how to screen for variation; and the location of those amino acids that play a critical role. Therefore, the skilled artisan is enabled to conduct routine experimentation following the instant specification to practice the claimed compounds.

The need to conduct routine experimentation does not form the basis for a rejection of the claims under 35 U.S.C. §112, first paragraph. Rather, it is if the skilled artisan would be required to conduct undue experimentation that underlies an enablement rejection.

6. Variants

The claims are rejected as requiring undue experimentation for reasons similar to those stated by the Examiner concerning "Diverse Peptides" as discussed *supra*. Again, Applicant respectfully maintains that the specification provides clear guidance to the skilled artisan as to the variations in amino acid sequence; how to screen for activity correlated to the amino acid sequence as well as which amino acids are critical to the immunomodulating activity.

7. Subtherapeutic dosage

The claims are rejected because the specification is not considered to have provided an adequate written description of the term "subtherapeutic dosage". Applicant traverses this rejection for the reasons as previously stated. The skilled artisan would be well aware of immunosupressants and their dosage. The term "subtherapeutic dosage" is defined at page 15, lines 13-15 and lines 18-24. (See text as cited *supra*.) The skilled artisan following the teachings of the specification would not require undue experimentation to practice the claimed methods.

8. Immunosuppressive agent

The Examiner apparently considers that the failure to limit the claims to requiring an immunosuppressive agent does not enable the claims. However, the specification provides clear guidance at page 15, lines 8-17 as to the types of immunosuppressive agents that may be employed. Further, the claims are now limited to a therapeutically effective regimen, which the skilled artisan could easily identify following routine experimentation.

9. Immunomodulating activity

The claims have been limited to lymphocyte immunomodulating activity. Therefore the skilled artisan would not require undue experimentation to practice the claimed invention in view of the specification's teachings as to how to screen for such activity.

10. Homodimer/Heterodimer

Applicant traverses the Examiner's rejection of the claims as lacking enablement. The skilled artisan in following the specification would not required undue experimentation to identify which sequences possess lymphocyte immunomodulating activity in view of the several assays taught as well as the identification of amino acids critical to this activity.

Rejection of the claims under 35 U.S.C. §103(a).

Claims 1-21 are rejected under 35 U.S.C. § 103(a) as obvious over Olsson (US PN 5,073,540) or WO88/05784.

Each of Olsson and WO88/05784 teach peptide sequences relating to alleles of the MHC Class 1 antigens.

Applicant respectfully traverses this rejection in view of the following remarks. Neither of these references teaches nor suggests the presently claimed dimeric compounds, methods of using or method of genetic expression to make. These references fail to teach the significance of the claimed sequence of amino acids as well as the significance of creating dimers of these sequences,

as presently claimed. Neither of the references teaches or suggest the acylation of the N-terminal nor do either of the references teach amidation or esterification of the C-terminal regions.

The Examiner concludes that it would have been obvious to one of ordinary skill in the art "to modify the prior art peptides and to test functional activity on surface receptors or lymphocyte activity of the modified peptides using the assays disclosed in Olsson or WO88/05784".

However, this conclusion fails to provide or refer to any motivation from within either reference to make such modifications in order to produce the claimed dimeric compounds. Without motivation to make these modifications, this rejection fails for lack of establishing a *prima facie* case of obviousness.

Applicant respectfully submits that these rejections may be properly withdrawn and the claims found allowable. If the Examiner considers that a telephone interview would be helpful in furthering the prosecution of this application, the Examiner is invited to contact the undersigned at the telephone number indicated below.

In the unlikely event that the transmittal letter is separated from this document and the Patent Office determines that an extension and/or other relief is required, applicant petitions for any required relief including extensions of time and authorizes the Assistant Commissioner to charge the cost of such petitions and/or other fees due in connection with the filing of this document to **Deposit Account No. 03-1952**. However, the Assistant Commissioner is not authorized to charge the cost of the issue fee to the Deposit Account.

Dated: December 19, 1997

Respectfully submitted,

By: _____

Thomas D. Mays, Ph.D., J.D.
Registration No. 34,524

Morrison & Foerster LLP
2000 Pennsylvania Avenue, N.W.
Washington, D.C. 20006-1888
Telephone: (202) 887-8761
Facsimile: (202) 887-0763